

Carcinogens and Cancers in Freshwater Fishes

by John J. Black* and Paul C. Baumann†

Epizootics of neoplasms in freshwater fish species are considered in relation to circumstantial and experimental evidence that suggest that some epizootics of neoplasia of hepatocellular, cholangiocellular, epidermal, and oral epithelial origin may be causally related to contaminant exposure. Although there is concern for the safety of consuming fish affected with neoplasms, this concern may be misdirected as direct transmission of cancer by ingesting cancerous tissue would seem unlikely. Of greater concern is the matter of toxic and cancer-causing chemicals present in edible fish that exhibit neoplasia as a symptom of past exposure via residence in a polluted waterway. There is ample evidence to suggest that contaminant chemicals ingested via contaminated Great Lakes fish may already be affecting both human and ecosystem health, but these effects are subtle and may require new approaches to the study of the affected systems.

Introduction

Fish neoplasia has recently received considerable emphasis as an early warning system for the detection of carcinogens in the aquatic environment (1,2). This idea is supported mostly by circumstantial evidence (1-5). There is, however, a growing body of field-related, laboratory-generated data, which also supports a link between certain kinds of aquatic pollution and cancer in fish (6-10). The present paper will not deal as much with the linkage of waterborne carcinogens as a causative agent of fish neoplasia, as with identifying the kinds of freshwater species affected with epizootic neoplasia, the anatomical sites and histologic types of neoplasms, prevalence data for specific geographic sites, and a review of information concerning levels of cancer-causing chemicals in these species. No attention will be given to detailed descriptions of the histologic picture or classifications of tumors in fish. Neoplasms in fish can vary widely in their degree of cellular atypia and biologic behavior. In the present paper, it is convenient to discuss these growths under the inclusive term "neoplasm," recognizing that such variation exists.

While we will not limit our discussion to Great Lakes fisheries, some emphasis will be given to fish cancer and contaminant problems of the Great Lakes and tributary waters. The title of the present conference emphasizes the potential of aquatic food resources as conveyers of chemical carcinogens to the human population. The conference title carries the implication that only those species used for commercial fisheries would be of interest. Our topic of discussion involves freshwater fish populations exhibiting neoplasia. Although most of the species

involved will not be subject to commercial fishing, all are consumed to some extent. The public is concerned about the safety of consuming cancerous fish *per se*. In a sense, this concern is misdirected. After all, it is possible to induce liver cancer in rainbow trout by exposing embryos to as little as 1 ng of aflatoxin B₁, yet in the adult tumor-bearing trout, the presence of the chemical that provoked the stimulus will not be detectable. It is conceded that the risk of transmitting cancer by ingesting cancerous fish tissue is an unknown. However, since most freshwater fish is cooked before being consumed, it is expected that risks of direct transmission of an oncogenic DNA fragment or virus would be unlikely. Rather, our concern here is for the ingestion of chemical contaminants in edible fish tissue. Particularly, this is of concern where cancerous fish are taken from heavily polluted water where they are chronically exposed to a wide range of chemical contaminants.

Fish Species Affected with Neoplasms

Of the more than 200 freshwater fish species there are probably no more than 50 freshwater fish species commonly kept by anglers. There are more than 80 freshwater fish species seldom kept by anglers. These include various lampreys, gars, minnows, killifishes, madtoms (small catfishes of the genus *Schilbeodes*), sculpins, darters, and several members of the herring family that are found in freshwater, e.g., gizzard shad. The freshwater locales and species where epizootics have been discovered do not usually foster or support major commercial fisheries. On the other hand, all of the species involved are edible and are consumed and fished commercially to some extent in other locations. Thus, there is always the possibility of migration of fish from heavily contaminated areas to cleaner areas where they may conceivably be taken in either a commercial or sport fishery.

Various kinds of neoplasms, including hepatic neoplasms, have been documented to occur in freshwater teleosts (Table 1),

*Roswell Park Memorial Institute, 666 Elm Street, Buffalo, NY 14263.

†U.S. Fish and Wildlife Service, NRCRC-Field Research Station, Ohio State University, Museum of Zoology, 1813 N. High Street, Columbus, OH 43210.

Address reprint requests to J. J. Black, Roswell Park Memorial Institute, 666 Elm Street, Buffalo, NY 14263.

Table 1. Epizootic neoplasms in freshwater fishes.

Species	Organs site/neoplasm type ^a	Geographic location	Reference
Black bullhead	Oral papilloma	Sewage pond Tuskagee, Alabama	(18)
Brown bullhead	Oral papilloma	Schuylkill River, Delaware ^b	(19)
	Oral papilloma	Lakes in Polk County, Florida	(11)
	Oral and epidermal papilloma	Western Great Lakes, inland lakes, New York	(20,21,28) (M. Wolfe, personal communication)
	Hepatocellular, cholangiocellular	Western Great Lakes, inland lakes, New York	(20,21)
Freshwater drum	Dermal melanoma	Sudbury River, Massachusetts, E. Lake Erie, and Upper Niagara River	(11)
		Sudbury River, Massachusetts, E. Lake Erie, and Upper Niagara River	(20)
		Finger Lakes, New York	(22)
Lake trout	Lateral line system ^c	Great Lakes Region	(23)
Muskellunge	Lymphosarcoma	Great Lakes Region	(23)
Northern pike	Lymphosarcoma	Great Lakes Region	(23)
Sauger	Hepatocellular	Torch Lake and Keweenaw Waterway, Houghton County, Michigan	(24)
Walleye pike	Hepatocellular, dermal fibroma	North America (?)	(25,26)
White sucker	Epidermal papilloma, hepatocellular, cholangiocellular	Great Lakes system	(20,27,28)
		Great Lakes system	(20,29)

^aNeoplasms exhibit a range of invasive potential from noninvasive to locally extensive invasion to an occasional neoplasm exhibiting metastatic growth.

^bHistorical data (1941); 166 tumor-bearing fish were studied (160/166 had oral tumors), indicating the tumors must have been common in these populations. Fish (40/166) also had epidermal tumors located at sites other than the mouth (e.g., barbels, head, body).

^cCell of origin is uncertain.

and the epizootiology of these diseases has recently been reviewed by Harshbarger and Clark (11). These authors have concluded on the basis of converging evidence from numerous investigations involving both field and laboratory data that liver neoplasms, and possibly epidermal neoplasms, in certain bottom-feeding species are most specifically correlated to exposure to chemical contaminants; e.g., historical (epizootic liver neoplasms found only after 1940); experimental carcinogen exposure (of the 30-odd carcinogens tested, all produced some liver neoplasms); physiological/biochemical evidence (metabolizing enzymes in the liver lead to DNA adducts); experimental carcinogenesis studies with contaminated sediment (skin painting, feeding of contaminated benthos to flounder, trout fry injections). The elegant studies of hepatic neoplasms in English sole (12-15) and more recently, investigations of hepatic neoplasms in winter flounder (16,17) are particularly supportive of the idea that neoplasms in some fish species are due to environmental contaminant exposure. Currently, there are no studies of environmental carcinogenesis in any freshwater species that are comparable to the extensive interdisciplinary investigations of the relationships between aromatic hydrocarbon pollution and hepatic neoplasia in marine flatfishes. On the other hand, it is likely that discoveries relevant to the relationships between aromatic hydrocarbon pollution and hepatic neoplasia in marine flat-fishes may well be applicable to fresh water environments having the same or similar sediment contaminant profiles.

Among the various freshwater species listed in Table 1, brown bullheads and white suckers appear circumstantially to be highly sensitive sentinel animals. Both fish species are bottom feeders and, at one or more locations, have exhibited oral, epidermal, and hepatic neoplasms.

White suckers (*Catostomus commersoni*) from some Great Lakes sites, in particular, western Lake Ontario, have exhibited high frequencies of oral papillomas. On the basis of a report by Sonstegard (27) of C-type virus particles observed by electron microscopy and tissue fractions containing reverse transcriptase activity, this neoplasm was suspected to have a viral etiology. No viruses were detected in subsequent ultrastructures studies conducted by Smith et al. (30). The development of these neoplasms may also be influenced by pollution, since the frequency of occurrence increases dramatically from a low of around 6% in the eastern basin, to a high of 39% in the western part of the basin near the Oakville-Burlington, Ontario, Canada, area (27).

Hepatic neoplasms of both cholangiocellular and hepatocellular origin also occur in white suckers. Dawe et al. (31) indicated that 3 of 12 white suckers from Deep Creek Lake, Maryland, had cholangiocellular neoplasms. It should be noted that only 5 of the fish examined by Dawe et al. were large adults, i.e., of a size/age range where frank neoplasms are normally observable. In other words, since cancer in fish, as in mammals, is an age-related disease, tumor prevalence comparisons must be on an age-adjusted basis. Thus, the incidence of this condition in Deep Creek Lake (3 of 5 adults) could have been quite high.

Hepatic neoplasms of both bile ductular and hepatocellular origin have been found to occur in the white sucker populations inhabiting the industrialized western basin of Lake Ontario, i.e., the liver neoplasms occurred in the same populations exhibiting high frequencies of oral papillomas (29). In these fish, bile duct neoplasms were present in 6% and hepatocellular neoplasms were present in 2 to 3% of suckers from the polluted Lake Ontario sites ($n = 456$) versus none in suckers from the control sites (Lake Simcoe and Lake Huron, $n = 108$). Both types of hepatic

neoplasms have also been observed in white suckers from polluted urban-industrial sites on eastern Lake Erie and the upper Niagara River, in the vicinity of Buffalo, New York (20). In addition, several cases of hepatic, gastrointestinal, and pancreatic neoplasms have been observed in fish of a related genus, *Moxostoma* sp., e.g., red horse suckers (20).

In brown bullheads, hepatic neoplasia, including hepatocellular and cholangiocellular types, have been observed to occur in bullheads from Deep Creek Lake, Maryland (31), the Fox River, IL (32), industrialized urban aquatic areas of eastern Lake Erie in the vicinity of Buffalo, New York (20), the Black and Cuyahoga Rivers near Cleveland, Ohio (33), and the St. Mary's River, Michigan (33). In both the Black and Cuyahoga, as well as the urban-industrial sites near Buffalo, sediments are known to be heavily contaminated with aromatic hydrocarbons (Table 2). Although circumstantial evidence of high sediment loadings of aromatic hydrocarbons to the presence of neoplasms is suggestive of a role for these chemicals, hepatic neoplasms have also been found to occur in brown bullhead populations from four of six ostensibly nonpolluted inland lakes and reservoirs sampled in the state of New York (M. Wolfe, unpublished data). Although these lakes are reputed to be nonpolluted, there may be naturally occurring carcinogens or as yet unrecognized sources of carcinogenic pollutants into these lakes. Also, it should be recognized that neoplasms that present a histologically similar picture can have different causes, e.g., viral skin papillomas of laboratory rodents look the same as chemically induced skin papillomas.

Recent work by Kurelec et al. (34), using ³²P-postlabeling methodology, indicates that generally similar quantities of hydrophobic DNA adducts were present in hepatic tissue from cyprinid fishes collected from both polluted (Sava River) and nonpolluted (Korana River) river environments in Yugoslavia. It should be noted that the levels of DNA adducts found in these nontumorous cyprinid fishes from two Yugoslavian rivers were much lower than levels detected in fish from polluted U.S. environments (8-10). Perhaps even more significantly, in the experiments conducted in the U.S., fish exposed in the laboratory to extracts of sediments containing high concentrations of aromatic hydrocarbons developed hepatic DNA adduct patterns that were virtually identical to those produced by ³²P-postlabeling analysis of hepatic DNA from wild, tumor-bearing fish collected from the same polluted environments used as the source of sediments (10; A. E. Maccubbin and J. J. Black, unpublished data). Epizootics of epidermal and oral neoplasms also occur in brown bullheads. To an extent, these epidermal and oral neoplasms tend to co-occur in sites where liver neoplasia has

also been found.

An interesting epizootic of both hepatic and dermal neoplasm was found in the case of sauger (*Stizostedion canadense*) and to a lesser extent, walleyes (*S. vitreum*), from Torch Lake and the connecting Keweenaw Waterway, Houghton County, Michigan (24). Torch Lake is a large, deep lake (surface area 1077 ha; mean depth 17 m; maximum depth 35 m) located in Michigan's upper peninsula. The area is rich in copper deposits, and mines and refining of copper were a major part of the area's economy. Since the turn of the century, copper ore, extracted from mines in the area, was crushed at mills located along the shore of this lake. Tailings dumped in the lake were later dredged from the lake and reprocessed when the price of copper rose enough to assure economic feasibility. The reprocessing continued until 1968, when the mills closed. Although no known chemical carcinogens have been found in high concentrations, the sediments contain high concentrations of some metals, including Cr, Ni, Zn, and especially copper. The copper ore reprocessing used a flotation process (in part) in which various combinations of wood creosote, pine tar, and other organic chemicals such as xanthates (dialkyl-dithiocarbonates) were used as frothing agents for the flotation of the finely milled copper particles.

Sauger from Torch Lake have nearly a 100% incidence of hepatocellular neoplasm [neoplasms present in 23 of 23 sauger examined in 1979-80, and in 54 of 55 large adult sauger sampled in 1983 (35)]. Walleyes examined from the Torch Lake in 1979-80 also exhibited hepatic neoplasms (hepatic neoplasms were present in 3 of 11 specimens.) Sampling of the walleye population in 1983 indicated very few hepatic neoplasms were evident, suggestive of a decreased prevalence between 1979 and 1983. In 1983, only 4 small hepatic neoplasms were found among 106 walleyes sampled from the entire Keweenaw Waterway, including 25 walleyes from Torch Lake.

The saugers from these waters were heavily parasitized with several species of larval trematodes (liver) and nematodes (heart, pericardial cavity, and mesenteries) (36). It is not known to what extent the parasitic injury contributes to the presence of either the dermal growths or the hepatic neoplasms, but any strict correlation to either was inapparent. In addition to a total of 66 sauger and 106 walleyes examined from the Torch Lake-Keweenaw system, 86 white suckers, 23 redhorse suckers, 21 brown bullheads, 90 yellow perch, 23 smallmouth bass, and 62 northern pike were also necropsied and examined for neoplasms (35). Neoplasms were not evident in any other species examined. The white suckers, redhorse suckers, and yellow perch are infected by many of the same parasites found in the sauger.

Table 2. Some observed tumor frequencies in brown bullhead in relation to aromatic hydrocarbon pollution.

Waterway	Hepatic neoplasia, %		Bile ductular, %	External tumors ^a	Sediment PAH ^b
	Altered foci	Hepatocellular			
Black River, 1982	19.2	32.2	37.2	13.5	81.0
<i>n</i>	121	121	121	193	
Cuyahoga River 1984-1987	23.1	11.5	11.5	12.4	9.4
<i>n</i>	52	52	52	145	
Buffalo River, 1983, 1986	38.8	5.5	11.1	22.6	6.7
<i>n</i>	36	36	36	53	
St Mary's River, 1984	16.7	8.3	8.3	0.0	1.8
<i>n</i>	12	12	12	68	
Old Woman's Creek, 1984-1988	10.0	0.0	0.0	1.7	0.45
<i>n</i>	10	10	10	230	
Buckeye Lake, 1982	0.0	0.0	0.0	1.5	0.07
<i>n</i>	10	10	10	78	

^aEpidermal and oral neoplasms.

^bCombined values of benzo(a)anthracene, benzo(a)fluoranthene, 3,4-benzo(a)pyrene in microgram per gram dry weight of sediment.

It may be relevant to note that the saugers constitute the only Torch Lake-Keweenaw Waterway fish population with members old enough to have been alive at or near the time that the ore reprocessing and active disbursement of organic chemical to the lake was ongoing. Regardless of these circumstances, no conclusions have been reached relative to the exact cause of the tumors in these fish.

Dermal neoplasms were also present among 23 of the 55 sauger examined from Torch Lake and 6 of 106 walleyes collected from the entire Keweenaw Waterway. The histologic appearance of these growths was consistent with a diagnosis of dermal (ossifying) fibrosarcoma. Similar growths are relatively common in walleye populations from various other locations (Lake Erie, Detroit River, Tittabwass River, Lakes in western Canada, etc.). Studies have shown that these neoplasms in walleyes from Lake Oneida, New York, appear to have a retrovirus etiology on the basis of evident virus particles (25), seasonal regression patterns (26), which may be related to temperature effects upon high reverse transcriptase activity in dermal sarcoma tissue (P.R. Bowser, personal communication), and demonstrated transmission of the disease in juvenile walleyes by cell-free extracts (P.R. Bowser, personal communication).

Fish Consumption

Viable freshwater commercial fisheries do exist, especially in the Great Lakes. For example, in 1982, the commercial fishing harvest for the Great Lakes exceeded 116 million pounds. Included in this statistic was approximately 64 million pounds from Lake Erie (37). In the upper portion of the Mississippi River, through the states of Minnesota, Wisconsin, and Iowa, the commercial catch alone totals nearly 3 million pounds per year (38). Approximately 44% of the catch from these waters is composed of bottom-feeding carp and buffalo. Some species harvested from freshwater (not included in the above catch statistics) are not consumed by humans but are used in the production of animal and pet feeds.

Although commercial fishing remains an important industry in some areas of the Great Lakes, more and more states are emphasizing the considerable economic value of sport and recreational fisheries over commercial fishing. In the Ohio and New York waters of Lake Erie, the commercial fishing has recently been eliminated through a buy out of the commercial fleet. As indicated above, the Great Lakes support major recreational and sport fisheries. At least two dozen species of fish are commonly caught by anglers from these waters. Walleye are a prized game and food fish, and stocks of catchable-size walleye in the western basin of Lake Erie are estimated to exceed 25 million fish (37). The sport/recreational catch of trout and Pacific salmon from the Great Lakes (in total, five species) easily exceeds 12 million pounds. The catch of trout and salmon in Lake Ontario taken by the open water (trolling) fishery alone is in excess of 2 million pounds (39). This is approximately equal to the combined commercial harvest of all species taken from that lake. This figure does not include sizable numbers of trout and salmon caught by anglers fishing from the lakeshore or the additional large harvest that takes place when these fish ascend tributary streams for spawning. The total of all sport and recreational fishing trips made in the U.S. in 1985 was estimated at 735,400,000; 1 lb of

fish per trip yields the same number in pounds (40).

In view of the steadily rising U.S. per capita consumption of seafood (15.4 lbs yearly in 1987), the role of commercial aquaculture can be expected to increase. Freshwater aquaculture is already a rapidly growing and important industry. Recent production figures are approximately 51×10^6 lbs for trout, 280×10^6 catfish, and 65×10^6 for crayfish (mostly wild captured in Louisiana), and an additional 20×10^6 of miscellaneous species are harvested (41). Disclosure of chemical contamination of fishery products resulting from aquaculture would undoubtedly undermine the faith of the consumer and would have significant impacts upon this developing industry.

Aquatic Contamination

It is a fact of life that most freshwater fish, especially those taken from the Great Lakes, carry variable quantities of trace contaminants in their tissues. It is well known that contaminants, especially chlorinated organics, accumulate in part as a function of the lipid content of the organism. The highest concentrations are reached in fatty species such as lake trout, which occupy the terminal predatory niches of their respective food chains. Consumable fish are unique in that they constitute the only large group of predatory species consumed by North Americans.

Although a compendium of all compounds identified in Great Lakes fish tissues is beyond the scope of the present discussion, some feeling for the magnitude of this problem may be gained from the following considerations. Studies by Hesselberg and Seelye (42) identified 476 compounds present in Great Lakes fish tissues (Table 3). Of these 476 compounds, 29 were isomers of polychlorinated biphenyls (PCBs), 9 were chlorinated pesticides, 15 were chlorinated industrial chemicals, 5 were polycyclic aromatics, and over 150 were oxygen-containing compounds (metabolites?) such as phenols, esters, and/or carboxylic acids. Lake trout from Lake Michigan and walleyes from Lake St. Clair contained the largest number of chemicals (167 and 215 compounds, respectively). Only 8 compounds were identified from hatchery-reared lake trout, used as controls (42). Currently, fish from Lake Ontario (Table 4) are considered to carry the highest amounts of many of these anthropogenic compounds (43). The dramatic concentrations of chlorinated hydrocarbons in Great Lakes fish result from only trace detectable amounts found in water. For some contaminants such as PCBs in lake trout and other salmonids, the gradient between concentrations found in water and the fish may exceed 1 million. Thus, to receive an equivalent dose of PCBs contained in a single meal of Great Lakes trout or salmon (assuming fish contains 1.5 mg PCB, water contains 3 ng/L, and assuming water is consumed at a rate of 5 L/day), a human being would have to drink Great Lakes water for more than 200 years. Thus, it is not surprising that several reports have indicated that Great Lakes fish are a major dietary source of exposure to these stable organochlorines (44,45). A joint U.S. National Research Council-Royal Society of Canada committee concluded that the human population living in the Great Lakes basin is exposed to and accumulates appreciably more toxic substances than other parts of North America (46).

Table 3. Great Lakes fish contamination problems at a glance.

Basin-wide problems
476 Compounds identified*
53 Halogenated
29 PCBs
9 Pesticides
15 Industrial byproducts?
5 PAHs
150 Oxygen-containing compounds
e.g., Phenols, esters, carboxylic acids
Aliphatic hydrocarbons
Sources
42 Compounds of concern (mostly polluted harbor areas near major cities)
Aerial transport
Worst-case scenarios:
Lake Ontario, Lake Michigan

*Only eight compounds were identified in clean water controls.

Although the presence of contaminants in the lakes has been well documented, the possible health effects of the contaminants upon biota, including man, is less well understood. Studies of fish-eating birds have shown effects ranging from complete reproductive failures in the late 1960s to congenital malformations in the late 1970s to gradual improvements in reproductive success in the 1980s (47). Work by Casterline et al. (48) has indicated that cleaned up organochlorine residues containing fractions derived from edible fish tissues were potent inducers of arylhydrocarbon hydroxylase (measured in TCDD equivalents) when tested in an *in vitro* bioassay using the H4IIE rat hepatoma cell line. Furthermore, recent work by Tillitt et al. (49), using the same bioassay in a blind study, has shown that not only are these residues accumulated in fish-eating birds from the Great Lakes, but the assay results were correlated to both the rates of deformities and colony (egg) mortality.

Consumption rates of contaminated fish (mostly salmon) by humans and the transfer of PCBs, a potential causative agent of these effects, has been well documented in serum, cord blood, and breast milk (50,51). Recent studies by Jacobson et al. of human health effects in relation to consumption of contaminated Great Lakes trout and salmon, have clearly shown that subtle neurological and growth deficits occurred in a dose-related fashion in exposed infants (52,53). The validity of the putative PCB-contaminated Great Lakes fish consumption-human health effects linkage in these studies was strengthened by independent observations of similar neurological deficits among a group of North Carolina infants that were correlated to the concentrations

of PCBs in breast milk, irrespective of fish consumption, as a possible route of maternal exposure to these compounds (54). A recent study by Daly et al. (55), in which laboratory rats were fed contaminated Lake Ontario salmon, was strongly supportive of the idea that subtle neurological effects resulting in measurable behavioral changes occur as a direct result of contaminant exposure through consumption of contaminated fish.

Aerial transport is a continuing source of many toxic contaminants (e.g., DDT, PCBs, TCDD), but in addition to this more or less global transport, in the Great Lakes there are 42 identified heavily polluted areas of concern. These are mostly industrialized areas in and around various cities/harbors located throughout the Great Lakes (46). Fish from these contaminated harbor areas often carry a broad range of industrial and anthropogenic compounds that are not present in fish from nonindustrialized parts of the Great Lakes ecosystem (56).

In many of these areas, a major problem involves in-place pollutants (contaminated sediments). Sediments from urban areas are often heavily contaminated with PAH compounds. Because PAHs are actively metabolized and excreted by fish, members of this class of compounds do not accumulate in fish to the same extent that chloroorganics do. Although PAH compounds can be detected in fish taken from areas heavily contaminated with PAHs, the most prevalent PAHs in edible fish tissue are low molecular weight, noncarcinogenic PAHs, with only trace amounts of carcinogens (21,57) and their metabolites (58). Limited data for PAH compounds in fish indicate that oily, bottom feeding fish such as carp do accumulate higher residue levels than less oily species (59). Conversely, PAH do accumulate to significant concentrations in benthic food chain organisms (57), which apparently lack or are deficient in the appropriate mixed-function oxidase enzymes. These benthic food chain organisms constitute a known, quantifiable route of PAH exposure to fish that use these organisms for food (60). Furthermore, there is ample evidence to suggest that, once ingested, PAHs can either be metabolized to biologically active metabolites that are covalently bound to cellular DNA and/or excreted as conjugates in the bile (57,61,62).

Some fishing occurs even in aquatic areas known to be badly polluted, despite fish consumption advisories or health warnings that have been issued by fisheries and/or health agencies. In some of these heavily contaminated urban areas, local anglers fish for and consume significant quantities of chemically contaminated fish. The consumption of these fish by anglers and potential

Table 4. Some contaminant concentrations

Chemical	Species	Location	Concentration	Reference
DDTs (total)	Coho salmon	Lake Ontario	0.80 µg/g	(43)
Dieldrin	Coho salmon	Lake Ontario	0.03 µg/g	(43)
cis-Chlordane	Coho salmon	Lake Ontario	0.05 µg/g	(43)
trans-Chlordane	Coho salmon	Lake Ontario	0.02 µg/g	(43)
Mirex	Coho salmon	Lake Ontario	0.14 µg/g	(43)
Photomirax	Coho salmon	Lake Ontario	0.08 µg/g	(43)
PCBs (total)	Coho salmon	Lake Ontario	2.89 µg/g	(43)
TCDD	Coho salmon	Lake Ontario	0.031 ng/g	(64)
PAHs	Brown bullhead	Black River	13,604 ng/g	(65)
	Miscellaneous species	Eastern Lake Erie	29,753 ng/g	J. J. Black, unpublished
	Crayfish	Hershey River, Michigan	30 %*	
	Insects	Hershey River, Michigan	100 %*	

*Concentrations given as a percentage of sediment values.

health risks associated with consumption of these contaminated fish has not been well studied. Ironically, in the most heavily polluted urban areas, heavily exposed bottom-feeding species such as carp, catfish, suckers, and freshwater drum often make up the bulk of the catch. Projected cancer risks associated with the consumption of contaminated sport and recreationally caught fish appear to be significant even at levels that fall below FDA action levels (63).

Conclusions

In conclusion, there is a chain of evidence to suggest that contaminants in aquatic systems are affecting the health status of aquatic organisms as well as the humans consuming contaminated fish from these systems. For the most part, the effects appear to be subtle, and the significance of these effects is not well understood. New approaches to the problems of recognizing and measuring these subtle effects will be required. Cancers in some species of fish from some locations appear to be wholly or partly due to exposure to xenobiotic chemicals. Although some neoplasms in fish may be large and relatively easy to detect, the initiating event involving the formation of DNA adducts and possible promoting effects of chronic exposure involve very subtle events. Against this background, the rationale for further studies of epigenesis in native fish populations is obvious.

REFERENCES

1. Fish Cancer Epidemics Oversight. Report of hearing before a subcommittee of the U.S. House of Representatives Subcommittee on Fisheries and Wildlife Conservation and the Environment, Committee on Merchant Marine and Fisheries, September 21, 1983. Serial No. 98-40, Government Printing Office, Washington, DC, 1984.
2. Black, J. J. Aquatic animal neoplasia as an indicator for carcinogenic hazards to man. In: Hazard Assessment of Chemicals: Current Developments, Vol. 3 (J. Saxena, Ed.), Academic Press, New York, 1984, pp. 181-232.
3. Couch, J. A., and Harshbarger, J. C. Effects of carcinogenic agents on aquatic animals: an environmental and experimental overview. *Environ. Carcinog. Rev.* 3: 63-105 (1985).
4. Black, J. J., Fox, H., Black, P., and Bock, F. Carcinogenic effects of river sediments in fish and mice. In: Water Chlorination: Chemistry, Environmental Impact and Health Effects, Vol. 5 (R. L. Jolly, R. J. Bull, W. P. Davis, S. Katz, M. H. Roberts, Jr., and V. A. Jacobs, Eds.), Lewis Publishers, Chelsea, MI, 1985, pp. 415-427.
5. Metcalfe, C. D., Cairns, V. W., and Fitzsimons, J. C. Experimental induction of liver tumors in rainbow trout (*Salmo gairdneri*) by contaminated sediment from Hamilton Harbor, Ontario. *Can. J. Fish. Aquat. Sci.* 45: 2161-2167 (1988).
6. Varanasi, U., Stein, J. E., Nishimoto, M., Reichart, W. L., and Collier, T. K. Chemical carcinogenesis in feral fish: uptake, activation, and detoxification of organic xenobiotics. *Environ. Health Perspect.* 71: 155-170 (1987).
7. Gardner, G. R. Histopathology of feral and experimental flounder exposed to contaminated harbor sediments. Proceedings of the 14th Annual Aquatic Toxicity Workshop, November 2-4, 1987, Toronto, Ontario. Canadian Technical Report of Fisheries and Aquatic Sciences No. 1607, 1988, p. 145.
8. Dunn, B. P., Black, J. J., and Maccubbin, A. E. ^{32}P -postlabeling analysis of aromatic DNA adducts in fish from polluted areas. *Cancer Res.* 47: 6543-6548 (1987).
9. Maccubbin, A. E., Black, J. J., and Dunn, B. P. ^{32}P -postlabeling detection of DNA adducts in fish from chemically contaminated waterways. *Sci. Total Environ.* 94: 89-104 (1990).
10. Varanasi, U., Reichart, W. L., and Stein, J. E. ^{32}P -postlabeling analysis of DNA adducts in liver of wild English sole (*Parophrys vetulus*) and winter flounder (*Pseudopleuronectes americanus*). *Cancer Res.* 49: 1171-1177 (1989).
11. Harshbarger, J. C., and Clark, J. B. Epizootiology of neoplasms in bony fish of North America. *Sci. Total Environ.* 94: 1-32 (1990).
12. Malins, D. C., Myers, M. S., and Roubal, W. T. Organic free radicals associated with idiopathic liver lesions of English sole (*Parophrys vetulus*) from polluted marine environments. *Environ. Sci. Technol.* 17: 679-685 (1983).
13. Malins, D. C., McCain, B. B., Brown, D. W., Chan, S., Myers, M. M., Landahl, J. T., Prohaska, P. G., Friedman, A. J., Rhodes, L. D., Burrows, D. G., Gronlund, W. D., and Hodgins, H. O. Chemical pollutants in sediments and diseases of bottom dwelling fish in Puget Sound, Washington. *Environ. Sci. Technol.* 18: 705-713 (1984).
14. Malins, D. C., Krahn, M. M., Myers, M. S., Rhodes, L. D., Brown, W. D., Krone, C. A., McCain, B. B., and Chan, S. Toxic chemicals in sediments and biota from a creosote-polluted harbor: relationships with hepatic neoplasms and other hepatic lesions in English sole (*Parophrys vetulus*). *Carcinogenesis* 6: 1463-1469 (1985).
15. Krahn, M. M., Rhodes, L. D., Myers, M. S., Moore, L. K., MacLeod, W. D., and Malins, D. C. Associations between metabolites of aromatic compounds in bile and the occurrence of hepatic lesions in English sole (*Parophrys vetulus*) from Puget Sound, Washington. *Arch. Environ. Contam. Toxicol.* 15: 61-67 (1986).
16. Murchelano, R. A., and Wolke, R. E. Epizootic carcinoma in winter flounder (*Pseudopleuronectes americanus*). *Science* 228: 587-589 (1985).
17. Gardner, G. R., Yevich, P. P., Malcolm, A. R., Rogerson, P. F., Mills, L. J., Senecal, A. G., Lee, T. C., Harshbarger, J. C., and Cameron, T. P. Tumor development in American oysters and winter flounder exposed to a contaminated marine sediment under laboratory and field conditions. In: *Aquatic Toxicology*, Vol. 11 (D. C. Malins and A. Jensen, Eds.), Elsevier, Amsterdam, 1987, pp. 403-404.
18. Grizzle, J. M., Melius, M. P., and Strength, D. R. Papillomas on fish exposed to chlorinated wastewater effluent. *J. Natl. Cancer Inst.* 73: 1133-1142 (1984).
19. Lucke, B., and Schlumberger, H. Transplantable epitheliomas of the lips and mouth of catfish. I. Pathology. Transplantation to anterior chamber of eye and into cornea. *J. Exp. Med.* 14: 397-408 (1941).
20. Black, J. J. Field and laboratory studies of environmental carcinogenesis in Niagara River fish. *J. Great Lakes Res.* 9: 326-334 (1983).
21. Baumann, P. C., Smith W. D., and Parland, W. K. Tumor frequencies and contaminant concentrations in brown bullheads from an industrial river and a recreational lake. *Trans. Am. Fish. Soc.* 116: 79-86 (1987).
22. Spitzbergen, J. M., Bowser, P. R., and Wolfe, M. J. Epizootic neoplasia of the lateral line system of lake trout in New York's Finger Lakes (abstract). AFS and Eastern Fish Health Workshop, Annapolis, MD, July 17-20, 1989.
23. Sonstegard, R. A. Studies on the etiology and epizootiology of lymphosarcoma in Esox (*Esox lucius* L.) and (*Esox masquinongy*). *Prog. Exp. Tumor Res.* 20: 141-155 (1976).
24. Black, J. J., Evans, E. D., Harshbarger, J. C., and Zeigel, R. F. Epizootic neoplasms in fishes from a lake polluted by copper mining wastes. *J. Natl. Cancer Inst.* 69: 915-926 (1982).
25. Walker, R. Virus associated with epidermal hyperplasia in fish. In: *Neoplasms and Related Disorders of Invertebrate and Lower Vertebrate Animals* (C. J. Dawe and J. C. Harshbarger, Eds.), Natl. Cancer Inst. Monogr. 31: 195-207 (1969).
26. Bowser, P. R., Wolfe, M. J., Fournay, J. L., and Wooster, G. A. Seasonal prevalence of skin tumors from walleye (*Stizostedion vitreum*) from Oneida Lake, New York. *J. Wildlife Dis.* 24: 292-298 (1988).
27. Sonstegard, R. A. Environmental carcinogenesis studies in fishes of the Great Lakes of North America. *Ann. N.Y. Acad. Sci.* 298: 261-269 (1977).
28. Smith, I. R., Ferguson, H. W., and Hayes, M. A. Histopathology and prevalence of epidermal papillomas epidemic in brown bullhead, *Ictalurus nebulosus* (Lesueur), and white sucker, *Catostomus commersoni* (Lecepede), populations from Ontario, Canada. *J. Fish Dis.*, in press.
29. Hayes, M. A., Smith, I. R., Crane, T. L., Rushmore, T. H., Thorn, C., Kocal, T. E., and Ferguson, H. W. Pathogenesis of skin and liver neoplasms in white suckers (*Catostomus commersoni*) from industrially polluted areas in Lake Ontario. *Sci. Total Environ.*, 94: 105-123 (1990).
30. Smith, I. R., Baker, K. W., Hayes, M. A., and Ferguson, H. W. Ultrastructure of malpighian and inflammatory cells in epidermal papillomas of white suckers *Catostomus commersoni*. *Dis. Aquat. Organ.* 6: 17-26 (1989).
31. Dawe, C. J., Stanton, M. F., and Schwartz, F. J. Hepatic neoplasms in native bottom-feeding fish of Deep Creek Lake, Maryland. *Cancer Res.* 24: 1194-1201 (1964).
32. Brown, E. R., Hazdra, J. J., Keith, L., Greenspan, I., Kwapinski, J. B. G., and Beamer, P. Frequency of fish tumors found in a polluted watershed as compared to nonpolluted Canadian Waters. *Cancer Res.* 33: 189-198 (1973).

33. Baumann, P. C., and Mac, M. J. Polynuclear aromatic hydrocarbons and tumors in brown bullheads from the Black and Cuyahoga Rivers—cause and effect? Proceedings of the 14th Annual Aquatic Toxicity Workshop, November 2-4, 1987, Toronto, Ontario, Canada (A. J. Nimi and K. R. Solomon, Eds.), Canadian Technical Report of Fisheries and Aquatic Sciences No. 1607, 1988.
34. Kurelec, B., Garg, A., Krca, S., Chacko, M., and Gupta, R. C. Natural environment surpasses polluted environment in inducing DNA damage in fish. *Carcinogenesis* 10: 1337-1339 (1989).
35. Black, J. J., and Evans, E. D. Project report to the U. S. EPA Great Lakes National Programs Office, Chicago, IL, 1984.
36. Spence, J. A. Report to Michigan Department of Natural Resources, Michigan Technological University, Houghton, MI, 1986, unpublished.
37. Great Lake Fishery Commission. Annual Report, 1982.
38. Wisconsin Department of Natural Resources.
39. New York State Department of Environmental Conservation.
40. Sport Fishing Institute, Washington, DC.
41. *Water Farming Journal*, Vol. 4, 1989.
42. Hesselberg, R. J., and Seelye, J. G. Identification of organic compounds in Great Lakes fishes by gas chromatography/mass spectrometry. Great Lakes Fishery Laboratory, Administrative Report No. 82-1, U.S. Fish and Wildlife Service, Ann Arbor, MI, 1977.
43. Clark, J. R., DeVault, D., Bowden, R. J., and Weisharar, J. A. Contaminant analysis of filets from Great Lakes coho salmon, 1980. *J. Great Lakes Res.* 10: 38-47 (1984).
44. Davies, K. Human exposure routes to persistent toxic chemicals in the Great Lakes basin: a case study. In: *Toxic Contamination in Large Lakes*, Vol. 1, Chronic Effects of Toxic Contaminants in Large Lakes. Proceedings of World Conference on Large Lakes (N. W. Schmidtke, Ed.), Lewis Publishers, Chelsea, MI, 1988, pp. 195-226.
45. Humphrey, H. E. B. Human exposure to persistent aquatic contaminants: a PCB case study. In: *Toxic Contamination in Large Lakes*, Vol. 1, Chronic Effects of Toxic Contaminants in Large Lakes. Proceedings of World Conference on Large Lakes (N. W. Schmidtke, Ed.), Lewis Publishers, Chelsea, MI, 1988, pp. 227-238.
46. National Research Council of the United States and The Royal Society of Canada. The Great Lake Water Quality Agreement, an Evolving Instrument for Ecosystem Management. National Academy Press, Washington, DC, 1985.
47. Peakall, D. B. Known effects of pollutants on fish eating birds in the Great Lakes of North America. In: *Toxic Contamination in Large Lakes*. Proceedings of World Conference on Large Lakes (N. W. Schmidtke, Ed.), Lewis Publishers, Chelsea, MI, 1988, pp. 39-54.
48. Casterline, Jr., J. L., Bradlaw, J. A., Puma, B. J., and Ku, Y. Screening of fresh water fish extracts for enzyme-inducing substances by aryl hydrocarbon hydroxylase induction bioassay technique. *J. Assoc. Off. Anal. Chem.* 66: 1136-1139 (1983).
49. Tilit, D. E., Ankley, G. T., Geisy, J. P., and Kevern, N. R. H4IIE Rat Hepatoma Cell Extract Bioassay Derived 2,3,7,8-Tetrachlorodibenzo-p-dioxin-equivalents (TCDD-EQ) from Michigan Waterbird Colony Eggs, 1986 and 1987. Report submitted to Michigan Department of Natural Resources, Department of Fisheries and Wildlife, Michigan State University, East Lansing, MI, 1988, unpublished.
50. Schwartz, P. M., Jacobson, S. W., Fein, G., Jacobson, J. L., and Price, H. A. Lake Michigan fish consumption as a source of polychlorinated biphenyls in human cord serum, maternal serum and milk. *Am. J. Public Health* 73: 293-296 (1983).
51. Jacobson, J. L., Fein, G., Jacobson, S. W., Schwartz, P. M., and Dowler, J. K. The transfer of polychlorinated biphenyls (PCBs) and polybrominated (PBBs) across the human placenta and into breast milk. *Am. J. Public Health* 74: 378-379 (1984).
52. Jacobson, J. L., Jacobson, S. W., Schwartz, P. M., Fein, G. G., and Dowler, J. K. Prenatal exposure to an environmental toxin: a test of the multiple effects model. *Dev. Psychol.* 20: 523-532 (1984).
53. Jacobson, S. W., Fein, G. G., Jacobson, J. L., Schwartz, P. M., and Dowler, J. K. The effect of intrauterine PCB exposure on visual recognition memory. *Child Dev.* 56: 853-860 (1985).
54. Rogan, W. J., Gladen, B. C., McKinny, J. D., Carreras, N., Hardy, P., Thullen, J., Tinglestad, J., and Tully, M. Neonatal effects of transplacental exposure to PCBs and DDE. *J. Pediatr.* 109: 335-341 (1986).
55. Daly, H. B., Hertzler, D. R., and Sargent, D. M. Ingestion of environmentally contaminated Lake Ontario salmon by laboratory rats increases their avoidance of unpredictable aversive nonregard and mild electric shock. *Behav. Neurosci.*, in press.
56. DeVault, D. S. Contaminants in fish from Great Lakes harbors and tributary mouths. *Arch. Environ. Contam. Toxicol.* 14: 587-594 (1985).
57. Black, J. J., Hart, Jr., T. F., and Evans, E. E. HPLC studies of PAH pollution in a Michigan trout stream. In: *Chemical Analysis and Biological Fate: Polynuclear Aromatic Hydrocarbons* (M. Cooke and A. J. Dennis, Eds.), Battelle Press, Columbus, OH, 1981, pp. 343-355.
58. Varanasi, U., and Gmur, D. J. Characterization of benzo(a)pyrene metabolites isolated from muscle, liver, and bile of a juvenile flatfish. *Carcinogenesis* 3: 1397-1403 (1982).
59. Black, J. J., Dymerski, P. P., and Zapisek, W. F. Environmental carcinogenesis studies in the western New York Great Lakes aquatic environment. In: *Aquatic Toxicology and Hazard Assessment* (D. R. Branson and K. L. Dickson, Eds.), American Society for Testing and Materials, Philadelphia, PA, 1981, pp. 216-224.
60. Maccubbin, A. E., Black, P. J., Trzeciak, P. J., and Black, J. J. Evidence for polynuclear aromatic hydrocarbons in the diet of bottom-feeding fish. *Bull. Environ. Contam. Toxicol.* 34: 876-882 (1985).
61. Varanasi, U., Stein, J. E., and Hom, T. Covalent binding of benzo(a)pyrene to DNA in fish liver. *Biochem. Biophys. Res. Commun.* 103: 780-787 (1981).
62. Maccubbin, A. E., Chidambaram, S., and Black, J. J. Metabolites of aromatic hydrocarbons in the bile of brown bullheads (*Ictalurus nebulosus*). *J. Great Lakes Res.* 14: 101-108 (1988).
63. Foran, J. A., Cox, M., and Croxton, D. Sport fish consumption advisories and projected cancer risks in the Great Lakes basin. *Am. J. Public Health* 79: 323-325 (1989).
64. O'Keefe, P., Meyer, C., Hilker, D., Aldous, D., Jelus-Taylor, B., Dillon, K., Donnelly, R., Horn, E., and Sloan, R. Analysis of 2,3,7,8-tetrachlorodibenzo-p-dioxin in Great Lakes fish. *Chemosphere* 12: 325-332 (1983).
65. Vassilaros, D. L., Stoker, P. W., Booth, G. M., and Lee, M. L. Capillary gas chromatographic determination of polycyclic aromatic compounds in vertebrate fish tissue. *Anal. Chem.* 54: 106-112 (1982).